

Comparison of Wound Healing with and without Adjuvant Topical Oxygen Therapy in Infected Diabetic Wounds

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ABSTRACT

Diabetes mellitus (D.M) is one of the main problems in health systems and a global public health threat that has increased dramatically over the past 2 decades. Patients with D.M are prone to multiple complications such as diabetic foot ulcer (DFU). Despite of the advantages of debridement, adequate debridement must always precede the application of topical wound healing agents, dressings or wound closure techniques. **Objective:** The objective of the study was to compare the efficacy of adjuvant topical oxygen therapy with conventional methods and conventional methods alone in management of infected diabetic wounds. **Study Design:** Randomized Control Trial. **Setting:** Surgical Unit III, Allied Hospital, Faisalabad. **Period:** 4 months from March to June 2017. **Methodology:** A total of 120 cases included in this study were admitted either through OPD or emergency ward. Group A (Topical oxygen therapy was given along with conventional methods). Group B (Only conventional methods of wound care were applied). All patients were given single dose IV antibiotic half an hour before induction of anesthesia. All diabetic patients were administered regular insulin to control blood glucose levels. Good debridement was done, removing all dead tissue. Simple available cellophane bag applied, sterilized with antiseptic solution, tailored according to size of affected part used tapped on open side of body of patient like tourniquet. 100% oxygen was given in bag with routinely available oxygen cylinder exposing whole affected part of body or limb. Oxygen in chamber was given for maximum one and a half hour twice daily in one sitting for 7-10 days. Gram positive, gram negative and anaerobic cover was given with antibiotics. Wound was washed daily with normal saline. After clinical improvement patient was discharged and called for follow up at outdoor on weekly basis initially and then fortnightly for 6 months. **Results:** Mean age was calculated as 49.56±7.02 and 49.11±6.59 years in group A and B respectively. 53.33% (n=32) in group A and 58.33% (n=35) in group B were males, while 46.67% (n=28) in group A and 41.67% (n=25) in group B were females. Comparison shows that 46.67% (n=28) in group A and 26.67% (n=16) in group B had efficacy; p value was calculated as 0.02 showing a significant difference. **Conclusion:** Efficacy of adjuvant topical oxygen therapy with conventional methods is significantly higher when compared with conventional methods alone in management of infected diabetic wounds. **Keywords:** Diabetes Mellitus, infected diabetic wounds, management, topical oxygen therapy.

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INTRODUCTION

Diabetes mellitus is the most common and serious metabolic disorder which due to angiopathy and neuropathy leads to chronic foot lesions and has a higher risk of amputations. Wound wash, debridement and dressings are conventional methods of wound management.^{1,8,11,12} In debridement, all devitalized tissue is removed. Wound washed with normal saline, hydrogen peroxide and pyodine solution. Repeated dressings with gels and chemical work by mechanism of chemical debridement. TOPOX (topical oxygen) therapy is the provision of 100% oxygen directly to an open moist wound under more than atmospheric pressure, that diffuses into wounds and increases local cellular oxygen tension, which in return promotes wound healing in the different ways such

as promoting angiogenesis, fibroblast activation, up regulation of growth factors, down regulation of cytokines, kills certain anaerobes, prevents growth of species such as pseudomonas.^{11,13,14,15} Prevents production and release of clostridia alpha toxin, and restores neutrophil mediated bacterial killing in previously hypoxic tissues. Iondahl study clearly support benefits of topical oxygen therapy where the TOPOX patients have significant benefits 52% VS. 29% of conventional methods alone¹. Also studies carried out earlier have shown that TOPOX therapy offers better results in the management of wounds due to diabetes, tuberculosis, venous ulcers, burns, gangrenous lesions etc.

The rationale of my study is to compare wound healing in diabetic patients with use of adjuvant TOPOX therapy along with conventional methods

and only conventional methods in our hospital. Local data is deficient regarding this technique and this is not in practice commonly. This study will provide recommendations to benefit patients regarding early healing and decreased morbidity.

METHODOLOGY

Study design: Randomized Control Trial.

Setting: Surgical Unit III, Allied Hospital, Faisalabad.

Period: 4 months from March to June 2017.

Sample size: Sample size: 120 (60 in each group).

Sampling technique: Non-probability consecutive sampling.

Inclusion criteria: All diabetic patients between the age of 15 and 60 years of either gender having infected wounds on any body part except face taking regular insulin.

Exclusion criteria: Advanced malignancy with metastasis. Patients who refused to take part. Patients with other co-morbid conditions like multi-organ failure.

RESULTS

A total of 120 cases (60 in each group) fulfilling the inclusion/exclusion criteria were enrolled to compare the efficacy of adjuvant TOPOX with conventional methods and conventional methods alone in the management of diabetic infected wounds. Age distribution of the patients shows that 13.33% (n=8) in group A and 11.67% (n=7) in group B were between 15-40 years of age while 86.67% (n=52) in group A and 88.33% (n=53) in group B were between 41-60 years of age, mean \pm SD was calculated as 49.56 \pm 7.02 and 49.11 \pm 6.59 years in group A and B respectively. (Table No. 1)

Table 1: Age distribution (n=120)

Age (in years)	Group A (n=60)		Group B (n=60)	
	No. of Patients	% of Patients	No. of Patients	% of Patients
15-40	8	13.33	7	11.67
41-60	52	86.67	53	88.33
Total	60	100	60	100
Mean \pm SD	49.56\pm7.02		49.11\pm6.59	

Gender distribution of the patients shows that 53.33% (n=32) in group A and 58.33% (n=35) in group B were male while 46.67% (n=28) in group A and 41.67% (n=25) in group B were females. (Table No. 2) Mean duration of diabetes mellitus was calculated as 6.7 \pm 3.11 years in group A and 6.58 \pm 3.06 years in group B (Table No. 3) Frequency of body parts involved shows that 78.33% (n=47) in

group A and 80% (n=48) in group B had feet involved while 21.67% (n=13) in group A and 20% (n=12) in group B involved hands. (Table No. 4)

Table 2: Gender distribution (n=120)

Gender	Group A (n=60)		Group B (n=60)	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Male	32	53.33	35	58.33
Female	28	46.67	25	41.67
Total	60	100	60	100

Table 3: Mean duration of diabetes mellitus (n=120)

Duration of Diabetes	Group A (n=60)		Group B (n=60)	
	Mean	SD	Mean	SD
	6.7	3.11	6.58	3.06

Table 4: Frequency of body parts involved (n=120)

Body Parts Involved	Group A (n=60)		Group B (n=60)	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Feet	47	78.33	48	80
Hands	13	21.67	12	20
Total	60	100	60	100

Comparison of efficacy of adjuvant TOPOX therapy with conventional methods and conventional methods alone in the management of infected diabetic wounds shows that 46.67% (n=28) in group A and 26.67% (n=16) in group B had efficacy while 53.33% (n=32) in group A and 73.33% (n=44) in group B had no efficacy, p value was calculated as 0.02 showing a significant difference. (Table No. 5)

Table No. 5: Comparison of the efficacy of adjuvant topical oxygen therapy with conventional methods and conventional methods alone in the management of infected diabetic wounds (n=120)

Efficacy	Group A (n=60)		Group B (n=60)	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Yes	28	46.67	16	26.67
No	32	53.33	44	73.33
Total	60	100	60	100

Effect modifiers like age gender, duration and control of diabetes mellitus and body parts involved were controlled by stratification and post stratification chi square test was applied (Table 6-9)

Table 6: Stratification for efficacy with regards to age

Age: 15-40	Efficacy		P Value
	Yes	No	
Group A	4	4	0.14
Group B	1	6	
Age: 41-60			0.05
Group A	24	28	
Group B	15	38	

Table 7: Stratification for efficacy with regards to gender

Male	Efficacy		P Value
	Yes	No	
Group A	15	17	0.07
Group B	9	26	
Female			0.16
Group A	13	15	
Group B	7	18	

Table 8: Stratification for efficacy with regards to duration of disease

1-5 Years	Efficacy		P Value
	Yes	No	
Group A	13	15	0.09
Group B	7	21	
>5 Years			0.12
Group A	15	17	
Group B	9	23	

Table 9: Stratification for efficacy with regards to part of body involved

Feet	Efficacy		P Value
	Yes	No	
Group A	23	24	0.01
Group B	12	36	
Hands			0.78
Group A	5	8	
Group B	4	8	

DISCUSSION

Diabetes mellitus is one of the main problems in health system and a global public health threat that has increased dramatically in past two decades.^{1,2,5,7} Patients with Diabetes mellitus are prone to multiple complications such as diabetic foot ulcer (DFU). Despite the advantages of debridement, adequate debridement must always precede the application of topical wound healing agents, dressings, or wound closure procedures.^{1,6,7,9,10} We planned this study with the view to compare wound healing in diabetic patients with use of adjuvant TOPOX with conventional methods and conventional methods alone in our hospital. This study may provide recommendations

to benefit patients regarding their early healing and decrease morbidity.

In our study, mean age was calculated as 49.56±7.02 and 49.11±6.59 years in group A and B respectively, 53.33%(n=32) in group A and 58.33% (n=35) in group B were male while 46.67% (n=28) in group A and 41.67% (n=25) in group B were female, comparison of efficacy of adjuvant TOPOX with conventional methods and conventional methods alone in the management of infected diabetic wounds shows that 46.67%(n=28) in group A and 26.67% (n=16) in group B had efficacy, p value was calculated as 0.02 showing a significant difference.

We compared our study with Londahl study which clearly supports benefits of topical oxygen therapy where the TOPOX therapy patients have significant benefits 52% VS. 29% of conventional methods alone. Also studies carried out earlier shows that TOPOX therapy offers better results in the management of wounds due to diabetes, tuberculosis, venous ulcers, burns, gangrenous lesions etc. Recent evidence, indeed, revealed that oxygen is not merely the primary source of energy, but also generates several ROS which may function as intracellular messengers in normal cell signal transduction and cell cycling.¹

Vickle et al. in a randomized controlled trial performed on patients with chronic DFUs, confirmed these findings by demonstrating that patients who received continuous TOPOX for 4 weeks had significantly higher wound size reduction as compared with patients who received standard wound care alone [87% (range: 55.7%-100%) VS. 46% (range 15%-99%); p < 0.05] The difference in the change in cytokines [IL -6, IL-8] and proteinase (MMP-1, -2, -9, TIMP-1) levels between the groups strengthened these results (p < 0.01) TOPOX opponents frequently cite a randomized controlled study conducted by Leslie et al. as clear evidence that TOPOX is not effective. This study, however, has serious methodological flaws.⁶ The most significant of these is that, although TOPOX does not penetrate to bone, a substantial rate of patients with findings suggestive of osteomyelitis were included in study [6 (50%) of the patients receiving TOPOX had abnormal bone scans or x-rays and above 70 mm/h sedimentation rate]

Kessler et al. hospitalized 28 diabetic patients with chronic non-healing wounds. Macro-vascular disease was excluded in all patients.⁷ Abidia et al. randomized 18 diabetic subjects with ischemic ulcers to receive 100% oxygen or air to breathe at 2-4 atm pressure for 90 min daily for 20 treatments. Complete healing 1 year after therapy occurred in 5 of 8 patients in the TOPOX therapy group and in 1

of 8 patients in control group. The relative risk of non-healing in the control group was 2.3. There was a significant decrease in wound area in treated group compared with control group.⁸ These findings support our results. However further studies in our population are required to validate these findings.

CONCLUSION

We concluded the efficacy of adjuvant TOPOX therapy with conventional methods is significantly higher than conventional methods alone in management of infected diabetic wounds.

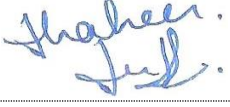

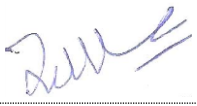
REFERENCES

1. Londahl M, Katzman P, Nilsson A, Hammarland C, Hyperbaric oxygen therapy facilities healing of chronic ulcers in patients with diabetes. *Diabetes Care*. 2010;33:998-1003.
2. Papanas N, Maltezos E, Edmonds M. Salvation of the diabetic foot: still for a quest for the Holy Grail? *Vasa* 2011;40:267-9.
3. Schreml S, Szeimes RM, Pranti L, Karrer S, Landthaler M, Bapilas P. Oxygen in acute and chronic wound healing. *Dermatol*. 2010;163:257-68.
4. Aragon-Sanchez J, Seminar review: a review of te basis of surgical treatment of diabetic foot infections. *Int J Low Extreme wounds*. 2011;10:33-65.
5. Lipsky BA, Peters EJ, Berendt AR, Semevile E, Bakker K, Embil JM. International working group on diabetic foot. Guidelines for treatment of Diabetic foot 2012;28:235-5.
6. Vickie VR, Kantarc A, Gu G, Hasturk H.A prospective, randomized clinical study evaluating the effect of

transdermal continuous oxygen therapy on biological processes and foot ulcer healing in persons with diabetes mellitus. *Ostomy Wound Manage*. 2013;59(11):19-26.

7. Kessler L, Bilbault P, Ortega F, Grasso C, Passemard R, Stephan D. TOPOX accelerates the healing rate of non ischaemic chronic DFUs: a prospective randomized study. *Diabetes Care* 2003;26:2378-82.
8. Abidia A, Laden G, Kuhan G, Johnson BF, Wilkinson AR. The role of Hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomized control trial. *Eur J Vasc Endovasc Surg* 2003;25:513-18.
9. Roe DF, Gibbins BL, Ladizinsky DA. Topical dissolved oxygen penetrates skin: model and method. *J Surg Res*. 2010;159:e29-36
10. Fantus, G. Diabetes, glucose toxicity. <http://www.endotext.org/diabetes/diabetes12new/diabetes12.htm> 2011
11. Duerden BI. Virulence factors in aerobes. *Clin Infect Dis*. 1994;18:S253-S259
12. Maiese K, Chong ZZ & Shang YC. Mechanistic insights into diabetes mellitus and oxidative stress. *Current medicinal chemistry*. 2007;16(16):1729-38
13. Hentges D. Anaerobes as normal flora. In: Finegold SM, Veorge W L, editors. *Anaerobic infections in humans*. San Diego, Calif: Academic Press, Inc 1989;37-53
14. Boulton AJ, Meneses P, Ennis WJ. Diabetic foot ulcers: a framework for prevention and care. *Wound rep Regen*. 1999;7:7-16
15. Laing P. Diabetic foot ulcers. *An J Surg*. 1994;167:31S-36S

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